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Sitting time, fidgeting and all-cause mortality in the UK Women's Cohort Study

Gareth Hagger-Johnson, PhD[1,2†], *Alan J. Gow, PhD[3,4†], Victoria Burley, PhD[5], Darren Greenwood, PhD[5,6] & Janet E. Cade, PhD[5]

[1]Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health, University College London, London, UK. Tel: +44(0)7445 212 399. E-mail: g.hagger-johnson@ucl.ac.uk

[2]Health and Social Surveys Research Group, Department of Epidemiology and Public Health, University College London, London, UK.

[3]Department of Psychology, School of Life Sciences, Heriot-Watt University, Edinburgh, UK.

[4]Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK.

[5]Nutritional Epidemiology Group, School of Food Science and Nutrition, University of Leeds, Leeds, UK.

[6]Division of Biostatistics, University of Leeds, Leeds, UK.

[†]These authors contributed equally to the manuscript.*Corresponding authors

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Author Contributions

GHJ and DG performed the statistical analysis. All authors contributed to writing the manuscript.

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Abstract

Introduction: Sedentary behaviours (including sitting) may increase risk of mortality independently of physical activity level. Little is known about how fidgeting behaviours might modify the association.

Methods: Data were drawn from the UK Women's Cohort Study. In 1999/2002, 12,778 women (age 37 to 78) provided data on average daily sitting time, overall fidgeting (irrespective of posture), and a range of relevant covariates including physical activity, diet, smoking status and alcohol consumption. Participants were followed for mortality over a mean of 12 years. Proportional hazards Cox regression models were used to estimate the relative risk of mortality in the high (vs. low) and medium (vs. low) sitting time groups.

Results: Fidgeting modified the risk associated with sitting time (p value for interaction = 0.04), leading us to separate groups for analysis. Adjusting for a range of covariates, sitting for 7+ hours/day (vs. <5 hours/day) was associated with 30% increased risk of all-cause mortality (HR = 1.30, 95% CI 1.02, 1.66) only among women in the low fidgeting group. Among women in the high fidgeting group, sitting for 5/6 (vs. <5 hrs/day) was associated with decreased risk of mortality (HR = 0.63, 95% CI 0.43, 0.91), adjusting for a range of covariates. There was no increased risk of mortality from longer sitting time in the middle and high fidgeting groups.

Conclusions: Fidgeting may reduce the risk of all-cause mortality associated with excessive sitting time. More detailed and better validated measures of fidgeting should be identified in other studies in order to replicate these findings and identity mechanisms, particularly measures that distinguish fidgeting in a seated from standing posture.

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Introduction

Current physical activity recommendations suggest that adults aged 18 to 64 years old should participate in about 150 minutes of moderate activity, or 75 minutes of vigorous activity (or some equivalent combination) per week for optimum health.[1] Even among adults who meet these recommendations and who sleep for eight hours per night, it is possible to spend over 15 hours a day being sedentary.

Sedentary behavior—defined as "as any waking behavior characterized by an energy expenditure ≤1.5 METs while in a sitting or reclining posture"[2] such as sitting or watching television[3] has come under increased scrutiny as a risk factor for mortality,[2, 4] needing independent consideration from low physical activity.[4, 5] Sedentary behavior has been shown to predict mortality and other health outcomes even in those achieving the WHO recommended physical activity levels.[2, 5-7]

A recent meta-analysis of 18 studies (two cross-sectional and 16 prospective) suggested that individuals who spent more time being sedentary had a greater likelihood of developing diabetes and CVD, and death from CVD or all-causes.[6] The associations were largely independent of physical activity[6]. Long-term follow-ups considering the effect of sedentary behavior on mortality are still relatively rare. Breaks in sitting time have been shown to improve metabolic biomarkers,[8, 9] but no study has examined whether fidgeting might modify an association between sitting time and all-cause mortality, the starting point for our investigation. Fidgeting is typically defined as involving small movements, especially of the hands and feet, often through nervousness, restlessness or impatience.[10] These movements can occur while seated or standing and might involve low levels of energy expenditure, but could bring benefits to those who are sedentary for long periods of time.

The current study examined the association between sitting time and mortality in almost 13,000 women in the UK Women's Cohort Study with an average of 12 years follow-up. Our aim was to determine if fidgeting modified the association between longer sitting times and mortality.

Methods

Study Sample

Data were drawn from the UK Women's Cohort Study (UKWCS), a prospective cohort study of women in England, Scotland and Wales.[11] At recruitment in 1995/98, 61,000 women aged 35 to 69 who had previously completed a survey from the World Cancer Research Fund were invited to complete a food frequency questionnaire (n = 35,372; 58% response rate) and provided socio-demographic information. In 1999/2002, 14,245 participants (aged 37 to 78) completed a second questionnaire which included questions on health behaviors, chronic disease, a 24-hour activity questionnaire, questions about physical activity levels, and fidgeting (each presented in that order). Ethical approval for the cohort was provided by 174 separate National Health Service (NHS) Committees. End of follow-up for our study was 31st December 2013; statistical analysis took place in 2014.

Measures

Mortality. Vital status was monitored using the NHS number assigned to each UK citizen. In our analysis, mortality was monitored from 1999/2002 (our baseline) to 31st December 2013 (end of follow-up).

Sitting time at baseline. Participants were asked ‘On an average weekday how is your day spent?’ They were then required to report the number of hours and/or minutes in a 24 hour day spent doing the nine activities: (Sleeping/Sitting/Light activities/Standing/Household chores/Lifting heavy objects/Light exercise/Moderate exercise/Strenuous) exercise, which included sitting. Participants were also asked ‘On an average weekend day how is your day spent?’ with the same response options. Answers for ‘Sitting’ were combined to give a mean average sitting time per day [(5*weekday + 2*weekend hours)/7]. The distribution was divided into three sitting time groups: low (<5 hours/day), medium (5 or 6 hours/day) and high (7 or more hours/day).

Fidgeting behavior at baseline. Participants were asked, ‘On a scale from 1-10 please indicate how much of your time you spend fidgeting. 1 would represent “no fidgeting at all” and 10 would represent “Constant fidgeting”’. The distribution was divided three fidgeting groups: low (1 or 2), middle (3 or 4), or high (5 to 10).

Covariates recorded at baseline. To record physical activity level, participants were asked, ‘Which of the following four activity classes best describes your present weekly activity?’ Response options were ‘No weekly physical activity (1)’, ‘Only light/moderate physical activity in most weeks (2)’, ‘Vigorous activity for at least 20 minutes once or twice a week (vigorous activity causes shortness of breath, rapid heart rate and sweating) (3)', 'Vigorous activity at least 20 minutes three or more times per week (4)'. Sleep time was recorded as one of the nine activities described above. Participants reported the number of hours they slept on an average weekday and weekend, combined to give a mean sleeping time per day [(5*weekday + 2*weekend hours)/7]. Participants were asked, 'In a typical week, how much do you drink?' Participants selected the relevant type of alcohol and reported amount consumed as 'Beer or cider (half pints each week)', 'Wine (glasses each week)', 'Sherry/Fortified Wines (glasses each week)', 'Spirits (glasses [singles] each week)'. Participants were also asked, 'If less than once per week, then...In a typical month how much do you drink?' with the same response options. Responses to either question were used to estimate units of alcohol consumed per week (1 UK unit = 8g ethanol), with those consuming 15 units or more per week classified as heavy drinkers, 1-14 units as moderate, and those reporting 0 units per week were coded as non-drinkers.[12] Self-reported smoking status was used to classify participants into current, ex, or never-smokers. Average daily fruit/vegetable consumption was calculated using responses to two questions: 'How many servings of vegetables or dishes containing vegetables (excluding potatoes) do you usually eat in an average week?' and 'How many servings of fruit or dishes containing fruit do you usually eat in an average week?' Participants were asked, 'Has a doctor ever told you that you have, or have had, any of the following conditions?' Chronic disease was defined as any 'Yes' response to the following: 'Heart attack, coronary thrombosis, myocardial infarction', 'Angina', 'Stroke,' 'Diabetes' or 'Cancer'. To record height and weight, participants were asked, 'Approximately how much do you weight at present?' (stones and pounds or kilograms) and 'What is your present height?' (feet and inches or centimetres). Responses were converted into kilograms and centimetres then were converted into Body Mass Index (BMI) categories using the standard formula and World Health Organisation criteria:[13] BMI

< 18.5 (underweight), BMI 18.5-24.99 (healthy weight), BMI 25-29.99 (overweight), BMI >=30 (obese).

Covariates recorded at recruitment. Participants reported any educational qualifications (None, CSE, GCE O Level, City & Guilds, A Level/Highers, Teaching diploma, HNC, Degree) which were grouped into the highest level achieved (none, secondary school, university degree). Occupational social class was coded from the participant's main job title (or partner's if missing) according to the NS-SEC method[14] and classified as professional/managerial (high), intermediate, or routine/manual (low). Women who reported not being in employment because they were retired, were classified as retired (vs. working).

Statistical analysis

In descriptive analyses, we evaluated differences in study variables across three sitting time groups. Cox regression with proportional hazards was used to evaluate the association between sitting time and mortality risk. The assumption of proportional hazards was tested by creating time-varying covariates (ln(T)*sitting time groups) where T was the follow-up time since exposure measurement. These variables were not significant for either the middle ($p = 0.32$) or high ($p = 0.88$) sitting time groups, showing that the proportional hazards assumption was not violated. In preliminary analyses, we tested whether fidgeting modified the association between sitting time and mortality. A model containing an interaction term between sitting time (in hours) and fidgeting groups fitted the data significantly better than a model containing only the separate effects for sitting time and fidgeting ($p = 0.04$) using the likelihood ratio test. This led us to separate the analytic sample into three fidgeting groups for analysis, to compare the association at different levels of fidgeting (low/medium/high). We also evaluated effects of the separate exposures and their joint effect, relative to the unexposed group. Analyses for all-cause mortality were conducted first in a minimally adjusted model (adjusting for age) and then in a fully adjusted model (adjusting for age, chronic disease, physical activity (none/vigorous twice weekly/vigorous 3+ times weekly vs. light/moderate), smoking (current vs. ex/never), alcohol use (heavy/non-drinker vs. moderate), daily fruit/vegetable consumption, daily sleep time, educational attainment, occupational social class and retirement. We did not adjust for BMI in the main analysis, because this may lie on the causal chain between the exposure and mortality. Missing data (on covariates only; 1.1%) were replaced using multiple imputation with 10 replications in Mplus in order to reduce bias and increase statistical power.[15, 16] Sensitivity analyses were undertaken to check whether results differed in complete case data, to evaluate possible reverse causation, to compare weekday/weekend sitting, to consider separately chronic disease categories as covariates, to consider the 24-hour recall measure of physical activity also available, and to consider a possible mediating role for Body Mass Index (BMI). Analyses were performed in Stata version 13.1 and Mplus version 7.2.

Results

The analytic sample comprised 10,937 women with data on sitting time, fidgeting, covariates and vital status (12,778 after multiple imputation). Compared to the study population at recruitment, the analytic sample was younger (51.4 vs. 56.9 years) and contained a higher proportion of women with degree-level educational attainment (30.8% vs. 12.5%). Characteristics of the analytic sample are shown in Table 1 across sitting time groups, and in Appendix Table 1 according to vital status (n = 577 deaths). Women in the highest third of sitting time tended to be slightly younger, fidgeted less, be current smokers, drink alcohol heavily, have a poor diet, sleep for longer, and perform vigorous physical activity <3 times per week. The largest proportion of women with no educational qualifications and routine occupations, however, was found in the low sitting time group. For reference, characteristics of study variables according to fidgeting groups are shown in Appendix Table 2. The high fidgeting group tended to be younger, sit for longer, comprised more cigarettes smokers, lower levels of physical activity, longer sleep times, higher levels of educational and higher social class positions.

Associations between sitting time and behavioral measures, before separating fidgeting groups, are shown in Appendix Table 3. The effects of the separate exposures and their combined effects, relative to the group unexposed to each exposure were: sitting time (HR per hour = 1.09, 95% CI 1.04, 1.14), middle vs. low fidgeting group (HR = 1.52, 95% CI 0.81, 2.84), high vs. low fidgeting group (HR = 1.47, 95% CI 0.87, 2.48), sitting time*middle fidgeting group (HR = 0.89, 95% CI 0.79, 1.00), sitting time*high fidgeting group (HR = 0.92, 95% CI 0.79, 1.01). The p value for the interaction term (sitting time*fidget group) was

0.04 in the overall model, combining all three groups, showing evidence of significant effect modification. These preliminary analyses led us to separate the fidgeting groups for the main analysis, which used the larger analytic sample.

Results from the Cox regression models are shown in Table 2. Among women with low fidgeting scores, sitting for 7+ hours/day (vs. <5 hours/day) was associated with a 43% increase in risk of all-cause mortality in age-adjusted models (HR = 1.43, 95% CI 1.14, 1.80). After additional adjustment for age, chronic disease, physical activity level, educational attainment, occupational social class, smoking, alcohol use, fruit/vegetable consumption, and sleep hours, the association was attenuated but remained (HR = 1.30, 95% CI 1.02, 1.66). No association was seen between sitting for 7+ hours/day and all-cause mortality in the middle (HR = 0.75, 95% CI 0.44, 1.29) or high (HR = 0.76, 95% CI 0.50, 1.15) fidgeting groups. An apparent association between sitting 5/6 hours/day and decreased mortality risk was significant in the high fidgeting group (HR = 0.63, 95% CI 0.43, 0.91) in the fully adjusted model. We evaluated the linear association for sitting hours/day in order to evaluate consistency of these results. This and other sensitivity analyses, listed in Appendix Table 4, suggested that our results were robust.

Discussion

Using data from almost 13,000 women in the UK Women's Cohort Study followed for an average of 12 years, we found that fidgeting modified the association between sitting time and mortality, independently of a range of covariates including physical activity level. We replicated existing findings that longer sitting times were associated with increased risk of all-cause mortality,[17-23] even among those meeting physical activity recommendations, but did not see this association in medium and high fidgeting groups. Fidgeting appeared to remove the association between longer sitting times and subsequent mortality. While physical activity guidelines are generally well-represented in public health campaigns, there has been limited consideration of the potential negative impact of sitting for long periods.[24] The current study therefore provides important information that while longer time spent sitting may have negative consequences, simple behaviors may have the potential to offset this.

The current study did not address the potential mechanisms underlying the association between sitting time and mortality, as our focus was on exploring whether fidgeting modified the association. There have been suggestions that periods of sitting may be associated with abnormal glucose metabolism and the metabolic syndrome,[4] though full explanatory pathways are still lacking. It is, however, necessary to understand sitting time, fidgeting movements and the physiological changes associated with these behaviors so that public health policies can be developed that provide guidance on the patterns of sitting that are best for health and life expectancy.[24] For example, it has been suggested that replacing sedentary behavior with standing or light-intensity physical activity might be beneficial in reducing disease risk and mortality at a population level, independently of moderate or vigorous physical activity.[6] The current results suggest that more complex movements of the hands and feet may be important to measure, in addition to level of physical activity.

The current study has a number of strengths and limitations. The cohort consists of a large sample followed over an extended period of time from midlife, comparable to those previously reported.[17] The cohort only contains women however, so replications will be necessary in samples of men and women. That said, there has been some indication that women may be more adversely affected by excessive sitting.[4] The current analysis considered a number of known confounders of the association between sitting time and mortality. We did not adjust for BMI in the main analysis because it is likely to lie on the causal chain between sitting and mortality,[6, 25] but we did consider the possible mediating role of BMI in supplementary analyses and found that this did not attenuate or mediate the association found.

The limited measure of fidgeting behavior available was an obvious limitation. We suggest it may act as a proxy for individuals who make small movements with the feet or hands, perhaps serving little practical function, but which bring benefits to those who sit for long periods of time. Low intensity physical movements may influence physiological processes even when below levels obtained during moderate or vigorous physical activities.[26] These movements may occur while standing or sitting, but it is the impact of low intensity movements throughout the day and particularly while seated that is of most interest for further study.[27] The validity of a single-item measure of fidgeting needs to be demonstrated rather than assumed, and so we encourage others to obtain more reliable and validated markers of fidgeting. Fidgeting has been of interest to researchers for many years.[28] It may be necessary to combine information from self-report,[29] tri-axial accelerometers,[30, 31] information about actual sitting position, and record specific limb movements, in order to obtain the most valid measures for this exposure.[31] Single item measures have been used in other studies, for example, in five studies in a recent meta-analysis which estimated a 34% higher mortality risk for adults sitting 10 h/day.[17] The main effect of sitting time was weak, although this may simply reflect heterogeneity of effect sizes known to occur across studies.[17] Weak main effects in the presence of effect modification are commonly found for various exposures and outcomes. Nonetheless, measurement error in the exposure and the proposed effect modifier, is likely to have led us to underestimate the true size of the association. Similarly, sitting time was only available as estimates for weekdays and weekend, rather than in different settings (such as occupational leisure time, commuting, etc.). When analysed separately, the findings for weekday/weekend sitting time were comparable in the low fidgeting group, but the overall association appeared to be stronger for weekend sitting than for weekday sitting. We were unable to distinguish between types of sitting (e.g. sitting at work, sitting at home)[5, 32, 33] but suggest that among women still working, weekend sitting may comprise more television watching,[3, 22] whereas weekday sitting may comprise more occupational sitting.[23] We were unable to adjust for other confounding factors such as long working hours and symptoms of common mental disorders such as anxiety and depression,[33] or longitudinal changes in sitting time and fidgeting. It has been suggested that sitting time and particularly television watching picks up other confounding factors,[34] such as additional 'snacking', alcohol consumption and smoking. We were not able to consider this possibility, but did control for the overall level of major health behaviors reported.

The current study represents a first attempt to examine how movements involved in fidgeting may protect against the adverse effects of sitting for long periods. Others have recommended that researchers revisit sitting time as an exposure in existing datasets.[4] We extend this call and additionally recommend that more detailed measures of fidgeting are also identified, with a view to replicating our study and extending it to elucidate possible mechanisms.

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Abbreviations

BMI: body mass index

CVD: cardiovascular disease

NHS: National Health Service

MVPA: Moderate or Vigorous Physical Activity

NS-SEC: National Statistics Socio-Economic Classification

UK: United Kingdom

UKWCS: UK Women's Cohort Study

Table 1

Table 1. Characteristics of study variables across tertiles of daily sitting time

	Daily sitting time				
	Low (0 to 4 hours)	Middle (5 to 6 hours)	High (7 to 17 hours)	P[a]	Total
	N = 4,622 (42.3%)	N = 3,501 (32.0%)	N = 2,814 (25.7%)		N = 10,937
Age (mean, SD)	55.7 (8.8)	56.6 (8.8)	54.0 (8.4)	<0.001	55.6 (8.8)
Fidgeting (%)	%	%	%		%
Low	56.5	52.9	50.8	<0.001	53.9
Medium	17.9	20.1	21.4	0.001	19.5
High	25.6	27.0	27.9	0.01	26.6
Current smoker	5.2	4.9	7.0	<0.001	5.6
Heavy alcohol drinker; >14/21 units alcohol/week, women/men	36.2	36.2	39.2	0.03	37.0
Poor diet; <5 fruits/vegetables per week	72.0	73.6	76.6	<0.001	73.7
Vigorous activity <3 times/week	77.5	81.6	85.3	<0.001	80.8
Sleep; <8 hours/day	50.7	51.0	57.5	<0.001	52.6
Chronic disease	12.4	13.6	11.8	0.72	12.7
Retired	12.0	13.3	8.3	<0.001	11.5
No educational qualifications	15.3	17.1	11.7	0.001	14.9
Routine occupation	30.3	33.6	33.0	0.01	32.0

Note. [a]P value for linear trend across tertiles of daily sitting time.

Table 2

Table 2. Association between sitting time and all-cause mortality, overall and stratified by fidgeting groups

	Fidgeting (1 = not at all, 10 = constantly)							
N = 12,778[a]	Low (1 or 2)		Middle (3 or 4)		High (5 to 10)		Overall	
Number of deaths (sitting <5,5/6,7+ hrs/day)	363 (125 / 134 / 104)		87 (32 / 38 / 17)		127 (51 / 46 / 30)		577	
	Age adjusted HR (95% CI)	Fully adjusted HR (95% CI)	Age adjusted HR (95% CI)	Fully adjusted HR (95% CI)	Age adjusted HR (95% CI)	Fully adjusted HR (95% CI)	Age adjusted	Fully adjusted
Sitting 5/6 hours/day (vs. < 5)	1.18 (0.96,1.45)	1.17 (0.95,1.45)	1.13 (0.75,1.73)	1.10 (0.72,1.68)	0.70 (0.49,1.00)	0.63 (0.43,0.91)	1.04 (0.88,1.22)	1.01 (0.85,1.19)
Sitting 7+ hours/day (vs. <5)	1.43 (1.14,1.80)	1.30 (1.02,1.66)	0.92 (0.54,1.54)	0.75 (0.44,1.29)	0.86 (0.58,1.29)	0.76 (0.50,1.15)	1.20 (0.99,1.44)	1.06 (0.88,1.29)

Note. [a]Missing data on covariates imputed. Fully adjusted = age, chronic disease, physical activity level, sitting time, educational attainment, occupational social class, retirement status, smoking (current vs. never/former), alcohol use (heavy and none vs. moderate), fruit/vegetable consumption, sleep hours.

Table 3

Table 3. Association between fidgeting and all-cause mortality in the high sitting time group and overall

	Sitting time			
	High (7+ hrs/day) n = 3,190		Overall n [a] = 12,778	
	Age adjusted HR (95% CI)	Fully adjusted HR (95% CI)	Age adjusted	Fully adjusted
Middle fidgeting group (vs. low)	0.62 (0.39,0.97)	0.57 (0.36,0.90)	0.83 (0.67,1.02)	0.82 (0.67,1.02)
High fidgeting group (vs. low)	0.80 (0.55,1.18)	0.74 (0.50,1.08)	1.00 (0.83,1.19)	0.95 (0.79,1.14)

Note. [a]Missing data on covariates imputed. Fully adjusted = age, chronic disease, physical activity level, fidgeting level, educational attainment, occupational social class, retirement status, smoking (current vs. never/former), alcohol use (heavy and none vs. moderate), fruit/vegetable consumption, sleep hours.

Appendix Table 1

Appendix Table 1. Characteristics of study variables according to vital status

	Alive	Dead
Age-adjusted proportions (95% confidence intervals)	N = 10,360	N = 577
Sitting time <6 hours/week	25.6 (24.8, 26.5)	24.5 (19.7, 29.3)
Low fidgeting group	53.7 (52.7, 54.6)	54.1 (48.8, 59.5)
Current smoker	5.2 (4.8, 5.7)	12.8 (9.2, 16.3)
Heavy alcohol drinker; >14 units alcohol/week for women	37.3 (36.3, 38.2)	33.6 (28.2, 39.0)
Poor diet; <5 fruits/vegetables per week	73.5 (72.7, 74.4)	76.4 (71.7, 81.2)
Vigorous activity <3 times/week	80.7 (79.9, 81.4)	82.4 (77.8, 87.0)
Sleep; <8 hours/day	52.7 (51.7, 53.6)	48.5 (42.9, 54.0)
Chronic disease	11.7 (11.1, 12.3)	34.1 (28.8, 39.4)
Retired	11.4 (10.8, 12.0)	10.8 (8.0, 13.5)
No qualifications	14.5 (14.0, 15.1)	18.6 (16.1, 21.1)
Routine occupation	32.0 (31.1, 32.9)	32.4 (27.4, 37.4)

Appendix Table 2

Appendix Table 2. Characteristics of study variables across fidgeting groups

	Fidgeting group				
	Low (1 or 2)	Middle (3 or 4)	High (5 to 10)	P[a]	Total
	N = 5,890 (53.9%)	N = 2,133 (19.5%)	N = 2,914 (26.6%)		N = 10,937
Age (mean, SD)	56.7 (9.0)	54.5 (8.4)	54.1 (8.2)	<0.001	55.6 (8.8)
Sitting 7+ hours/day	24.3	28.2	26.9	0.002	25.7
Current smoker	5.2	5.4	6.4	0.03	5.6
Heavy alcohol drinker; >14/21 units alcohol/week, women/men	36.4	37.8	37.5	0.24	37.0
Poor diet; <5 fruits/vegetables per week	73.7	74.5	73.0	0.57	73.7
Vigorous activity <3 times/week	81.3	82.7	78.4	0.004	80.8
Sleep; <8 hours/day	50.3	52.2	57.3	<0.001	52.6
Chronic disease	12.7	12.4	12.6	0.85	12.7
Retired	11.3	11.4	11.9	0.47	11.5
No educational qualifications	17.1	13.5	11.4	<0.001	14.9
Routine occupation	30.7	33.5	33.6	0.003	32.0

Note. Values are percentages unless shown otherwise. [a]P value for linear trend across fidgeting groups.

Appendix Table 3

Appendix Table 3. Association between sitting time, other health behaviours and all-cause mortality

N = 12,778	Overall	
	Age adjusted	Fully adjusted
Sitting 5/6 hours/day (vs. < 5)	1.04 (0.88,1.22)	1.01 (0.85,1.19)
Sitting 7+ hours/day (vs. <5)	1.20 (0.99,1.44)	1.06 (0.88,1.29)
Sleep hours	1.03 (0.96,1.11)	1.03 (0.96,1.11)
No weekly physical activity (vs. light/moderate physical activity)	1.35 (1.02,1.78)	1.35 (1.02,1.78)
Vigorous activity for at least 20 minutes once or twice a week (vs. light/moderate physical activity)	0.77 (0.63,0.94)	0.77 (0.63,0.94)
Vigorous activity at least 20 minutes three or more times per week (vs. light/moderate physical activity)	0.76 (0.60,0.97)	0.76 (0.60,0.97)
Current smoker (vs. non-smoker)	1.45 (1.27,1.65)	1.45 (1.27,1.65)
Fruit/vegetable consumption	0.96 (0.92,1.01)	0.96 (0.92,1.01)
Heavy alcohol consumption (vs. moderate)	0.86 (0.72,1.02)	0.86 (0.72,1.02)
No alcohol consumption (vs. moderate)	1.18 (0.97,1.42)	1.18 (0.97,1.42)

Note. [a]Missing data on covariates addressed with multiple imputation. Fully adjusted = age, chronic disease, physical activity level, sitting time, educational attainment, occupational social class, retirement status, smoking (current vs. never/former), alcohol use (heavy and none vs. moderate), fruit/vegetable consumption, sleep hours.

Appendix Table 4. Sensitivity analyses

Concern	Comments
• Linear association for sitting time in hours	• In fully adjusted models, a linear association between each additional hour of sitting time per day and all-cause mortality was only seen in the low fidgeting (HR = 1.07, 95% CI 1.02, 1.12) but not the middle (HR = 0.93, 95% CI 0.84, 1.04) or high (HR = 0.98, 95% CI 0.90, 1.06) fidgeting groups. The association between each additional hour of sitting time and all-cause mortality in the low fidgeting group was seen even among those at the highest level of physical activity (HR = 1.14, 95% CI 1.00, 1.30; N = 1111).
• Comparison with complete case data	• Reran analyses on complete case data, without imputation for missing data on covariates. Results were not materially different.
• Reverse causation	• We excluded deaths within the first five years of follow-up. Results were very similar, addressing concerns about reverse causation.
• Differences in weekday vs. weekend sitting	• The association between each additional hour of sitting among the low fidgeting group was nearly identical for weekday (HR = 1.07, 95% CI 1.02, 1.11) and weekend sitting (HR = 1.07, 95% CI 1.02, 1.12). We observed, however, that weekend sitting became significant when all fidgeting groups were combined (HR = 1.04, 95% CI 1.00, 1.08), whereas weekday sitting (or total sitting; reported above) was not (HR = 1.03, 95% CI 0.99, 1.06). The specificity of the association seen for weekend sitting might reflect different kinds of sitting behaviour undertaken at weekends, such as longer time for television watching, or genuinely smaller effect sizes for weekday sitting for other reasons. Our overall conclusions were unchanged.
• Chronic disease as a single category	• Replacing chronic disease with an indicator for each disease separately did not influence results.
• Alternative measure available of physical activity	• We also created an alternative measure of physical activity level using 24-hour recall of ‘Moderate’ and ‘Strenuous’ activities. These data were not used in the main analysis because they corresponded less well with established physical activity guidelines, but allowed us to compare results using two different methods. Results were

	very similar and did not change our conclusions.
• Body Mass Index as a possible mediator	• Additional adjustment for underweight, overweight or obesity (all vs. healthy weight) in the subsample of 9,606 women with data available on BMI did not attenuate the association between sitting time and mortality in the low fidgeting group. Similarly, additional adjustment for BMI as a continuous variable after excluding underweight women had little effect on the association.
• Main effect of sitting (i.e. effects in the reference category of the effect modifier)	• The association minimally adjusted for age (OR = 1.07, 95% CI 1.16, 1.25) was attenuated following additional adjustment for covariates (OR = 1.03, 95% CI 0.92, 1.15), consistent with interpretation of a weak or null main effect.